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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Takahiko Ishiguro

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EXAMINER

SHAW, AMANDA MARIE

ART UNIT

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 09/904,557	<b>Applicant(s)</b> ISHIGURO ET AL.	
	<b>Examiner</b> AMANDA SHAW	<b>Art Unit</b> 1634	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 29 February 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 13-15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 13-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 September 2007 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

1. This action is in response to the amendment filed February 29, 2008. This action is made FINAL.

Claims 13-15 are currently pending. Claims 13 and 14 have been amended.

Claims 13-15 are addressed herein.

### ***Claim Rejections - 35 USC § 102***

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 13 is rejected under 35 U.S.C. 102(b) as being anticipated by Hayes (Journal of Clinical Pathology 1999) as evidenced by Kondo (US Patent 5853981 Issued 12/1998).

Regarding Claim 13A Hayes teaches a method which comprises obtaining RNA transcripts from human individuals infected with EBV. In the instant case the “selected DNA molecule” is the EBV genomic sequence (page 99 col 1&2 and page 100 col 1).

Regarding Claim 13B Hayes teaches screening selected portions of the EBV genomic sequence. The selected portions are regions that encode homologues to important human proteins. Specifically the regions encode the vIL-10, BDLF2, and

BARF1 proteins (table 3). The nucleotide sequence of each of these regions is known. The purpose of this study was to determine which regions were expressed in different types of EBV infections (page 98 col 1).

Regarding Claim 13i Hayes teaches that the RNA transcripts were amplified using first and second primers. To amplify vIL-10 the first primer was complementary to 19 continuous nucleotides located at or near the 3' end of the selected portion of the selected DNA molecule, and the second primer was complementary to 23 continuous nucleotides located at or near the 5'-end of said selected portion of said selected DNA molecule (table 3 oligo 1.1 and 2.1).

Regarding Claims 13(i)(a-d) Hayes does not specifically recite each step of NASBA amplification, however as evidenced by Kondo NASBA comprises (a) forming a RNA-DNA duplex comprising one of the RNA transcripts and a complementary DNA molecule, by synthesizing a first DNA molecule complementary to the RNA transcript using a primer, an RNA-dependent DNA polymerase and one of the RNA transcripts (Column 4, lines 17-25); (b) preparing a single-stranded DNA molecule by hydrolyzing the RNA transcript of the RNA-DNA duplex using ribonuclease H (Column 4, lines 26-29); (c) forming a doubled-stranded DNA molecule comprising the single stranded DNA molecule of (b) and a complementary DNA molecule thereto, by synthesizing a second DNA molecule using a primer with a promoter sequence, a DNA-dependent DNA polymerase, and the single-stranded DNA molecule of (b) as a template (column 4, lines 30-38); (d) forming an RNA transcription product using an RNA polymerase, wherein RNA transcription is primed from the RNA-transcriptable promoter sequence

(column 4, lines 39-42); and (e) repeating steps (a) to (d) using the RNA transcription product of (d) as a template for the formation of the RNA-DNA duplex of (a) column 4, line 43-column 5, line 5). In the instant case the limitations recited in Claim 13 a-d are considered to be an inherent property of the NASBA method as demonstrated by Kondo.

Regarding Claim 13(ii) Hayes teaches that the amplification products were detected to thereby screen for a RNA transcript that is encoded by the selected portion of the selected DNA molecule (page 100 col 1).

Regarding Claim 13C, Hayes teaches a method of screening at least 3 selected portions of the EBV DNA molecule. Each portion (i.e. vIL-10, BDLF2, and BARF1) is different from, non overlapping, and adjacent to the other portions (table 3). In the instant case the phrase “adjacent to” has not been defined in the specification and the specification does not provide any guidance for determining whether two genomic regions are adjacent. As such the phrase “adjacent to” is being given its broadest reasonable interpretation. Therefore the vIL-10 gene, BDFL2 gene, and BARF1 gene are considered to be adjacent to one another since they are all located on the same genomic DNA molecule.

### ***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hayes (Journal of Clinical Pathology 1999), as evidenced by Kondo (US Patent 5853981 Issued 12/1998) as applied to claim 13 above, and further in view of Ishiguro (Nucleic Acids Research 1996).

The teachings of Hayes are presented above.

Regarding Claims 14 and 15 Hayes teaches a method wherein the amplification product is detected using a probe which consists of a sequence that is not complementary to either the first or second oligonucleotide primer (table 3), however Hayes does not teach that the probe is labeled with an intercalating fluorescent dye. Further Hayes does not disclose an intercalating fluorescent dye that has a differential

fluorescence characteristic depending on whether said probe exists in an unbound single-stranded state or in a bound duplex with said amplification product.

However Ishiguro teaches a fluorescent intercalative dye-labeled probe which can recognize a specific nucleic acid sequence by linking a fluorescent intercalative dye as a label to a single-stranded oligonucleotide complementary in nucleic acid sequence to a specific nucleic acid sequence of the specific nucleic acid, so that when the single-stranded oligonucleotide hybridizes with the specific nucleic acid, the intercalative dye intercalates into the resulting double-stranded oligonucleotide to alter the florescent property (Abstract).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Hayes by using probes linked to fluorescent intercalative dyes as suggested by Ishiguro. One would have been motivated to use the probes described by Ishiguro since they enable detection and quantification of nucleotide specific hybrids, not just any double stranded hybrid (page 4994, col 2 to page 4995 col 1). Further all of the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Additionally these claims would have been obvious because substitution of the probe taught by Hayes for the probe taught by Ishiguro would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

### ***Response To Arguments***

4. In the response filed February 29, 2008, Applicants amended claim 13 to recite that the at least one selected portion of the selected DNA molecule is also adjacent to the selected portion of B. The Applicants argue that in view of this amendment the claims can no longer be rejected under 35 USC 102 for being anticipated by Hayes because Hayes does not disclose the amplification of adjacent DNA portions. This argument has been fully considered but is not persuasive. In the instant case the phrase "adjacent to" has not been defined in the specification and the specification does not provide any guidance for determining whether two genomic regions are adjacent. However the Merriam Webster dictionary defines adjacent as (a) not distant; (b) having a common endpoint or border; or (c) immediately preceding or following. As such the phrase "adjacent to" is being given its broadest reasonable interpretation. Therefore the vIL-10 gene, BDFL2 gene, and BARF1 gene are considered to be adjacent to one another since they are all located on the same genomic DNA molecule even though they have intervening sequences between them. This broad interpretation is actually supported by the specification (page 14) which recites that "it is effective for improving working efficiency to exclude a specific region which is present in a region already known as a gene expression region by previous studies and a specific region which is present in a region that is obviously not a gene expression region based on its DNA sequence. This teaching demonstrates that the regions being examined can have intervening sequences between them. Therefore this rejection is maintained.

Regarding the rejection made under 35 USC 103(a) over the combination of Hayes (as evidenced by Kondo) and Ishiguro has also been traversed because the Applicants believe that Ishiguro does not compensate for the deficiencies of Hayes. The Applicants arguments over Hayes are discussed above. This rejection is maintained.

### **Conclusion**

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 7:30 TO 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for

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the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amanda M. Shaw  
Examiner  
Art Unit 1634

/Juliet C Switzer/

Primary Examiner, Art Unit 1634